# Controversies in Screening for Angle Closure Glaucoma

# 筛查闭角型青光眼的争议

13th Medical HK-Beijing conference
Wenzhou
22 October 2011

Jimmy Lai (黎少明)
*Eye Institute*
*The University of Hong Kong*
香港大學眼科研究所


# Cardinal Principles for Disease Screening (WHO)
# 世卫指引筛查疾病重要原则

1. Disease (疾病)- important health problem (重要健康问题) with recognizable pre-symptomatic state (可识别症状出现时状态)
2. Screening procedure (筛查方法)– acceptable to public and health care professionals (公众及医护人员可接受)
3. Treatment (治疗)- safe(安全), effective (有效) and universally agreed (普遍同意)
4. Economic cost of early diagnosis and treatment < total health care expenditure for leaving the disease untreated (及早确诊和治疗经济成本少于留下疾病的未经处理致盲后所需的总医疗开支)

# Screening for Diabetic Retinopathy
# 糖尿病视网膜病变筛查

## Important health problem
## 重要健康问题

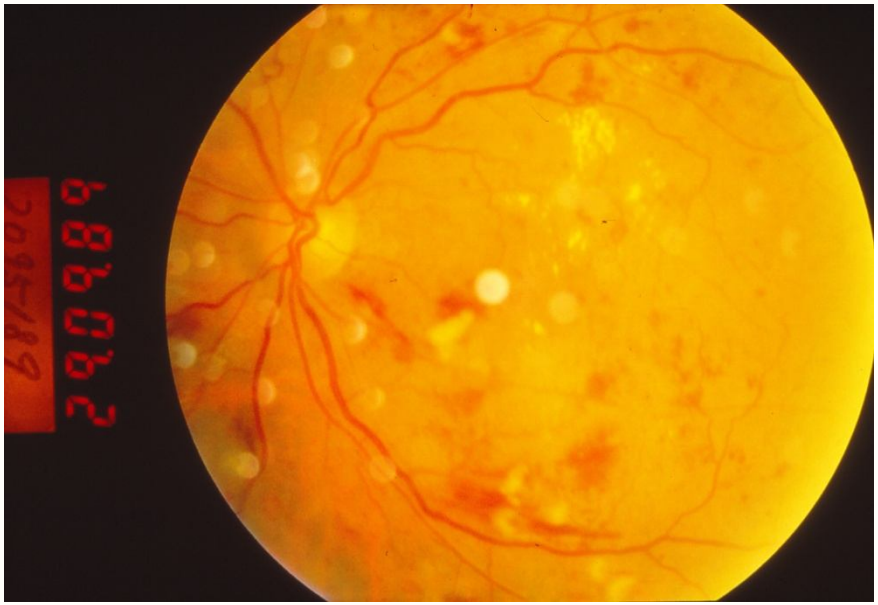
- Diabetes mellitus (糖尿病) affects 2% of the population (10-15% type 1, remainder type 2) (糖尿病影响的人口的2％)
- Prevalence of retinopathy (糖尿病视网膜病变流行程度): 10 years after diagnosis 40-50% and after 20 years 90%
- Diabetic retinopathy - commonest cause of blindness in the working age population in many countries (在许多国家的劳动年龄人口失明的最常见的原因)

# Screening for Diabetic Retinopathy
# 糖尿病视网膜病变筛查

## Recognizable pre-symptomatic state

## 可识别症状出现时状态

- Well defined group (明确的一羣)- DM subjects
- Easily recognized disease state(容易识别的疾病状态)- diabetic retinopathy



# Screening for Diabetic Retinopathy
# 糖尿病视网膜病变筛查

**Screening procedure – acceptable to public and health care professionals**

筛查程序公众及医护人员可接受

- Mydriatic retinal digital imaging (数码眼底相机)
- Annual examination (每年检查) beginning 5 years after diagnosis (type 1) and at time of diagnosis (type II)

# Screening for Diabetic Retinopathy
# 糖尿病视网膜病变筛查

## Treatment (治療)

Natural course of disease (疾病自然过程):

- Diabetic Retinopathy Study (DRS)
- Early Treatment of Diabetic Retinopathy Study (ETDRS)
- Diabetic Retinopathy Vitrectomy Study (DRVS)

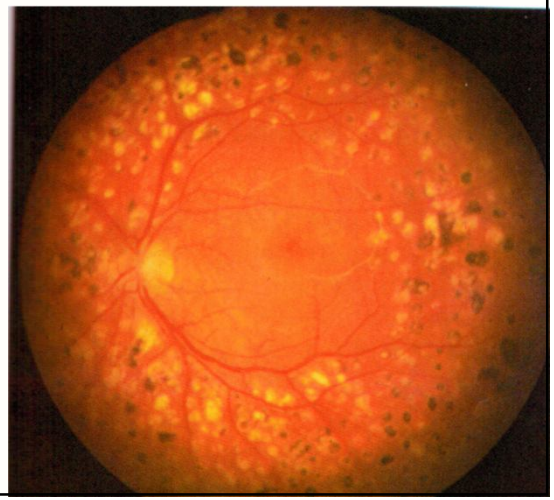
Contributed to understanding the natural course, risk factors and provided guidelines for the management of diabetic retinopathy (对疾病自然过程,危险因素有贡献.对糖尿病视网膜病变护理作指引)

# Screening for Diabetic Retinopathy
## 糖尿病视网膜病变筛查

**Treatment - safe, effective and universally agreed**

治疗安全有效及世界认同

- Beneficial effect of laser treatment (激光治疗的有益作用)established (确认)by DRS and ETDRS
- Laser photocoagulation prevented visual loss (防止视力丧失) in patients with proliferative diabetic retinopathy and macular oedema by about 50% compared with no treatment
- Facilities for laser treatment widely available in many developed countries (激光治疗在许多发达国家广泛设施)



# Screening for Diabetic Retinopathy
## 糖尿病视网膜病变筛查

Economic cost of early diagnosis and treatment

及早确诊和治疗经济成本

- Screening for diabetic retinopathy saves vision at a relatively low cost < disability payments provided to people who go blind in the absence of a screening programme
- (及早确诊和治疗经济成本少于留下疾病的未经处理致盲后所需的总医疗开支)

# Screening

## Diabetic retinopathy

- Symptom free at early retinopathy
- Retinopathy may be well advanced before visual symptoms noticed
- Preventive treatment should be given when they are symptom-free
- *Strong argument for establishing a screening programme

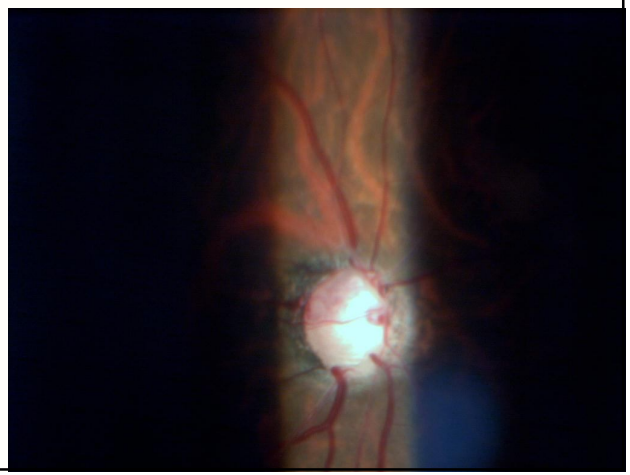
## Angle closure glaucoma

- Symptom free at PAC
- PACG may be well advanced before visual symptoms noticed
- Preventive treatment should be given when they are symptom-free (有症状之前应给予预防性治疗)
- Strong argument for establishing a screening programme? (建立筛选程序的强有力的论据)

# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

Argument for establishing a screening programme:

- Angle closure is a progressive disease that can lead to glaucoma 闭角是一个渐进的的条件,可导致青光眼
- Symptom free at PAC
- PACG may be well advanced before visual symptoms noticed 在视觉症状注意到前PACG可能已經很嚴重
- Preventive treatment should be given before glaucoma develops在青光眼发展前，应给予预防性治疗

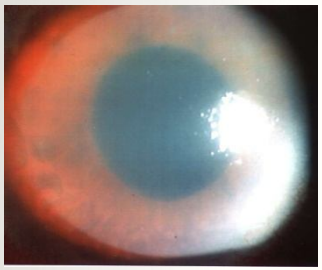


# Screening for angle closure glaucoma
# 筛查闭角型青光眼

Obstruction of trabecular meshwork by peripheral iris

**LPI**

ALPI
Lens/early
cataract extraction

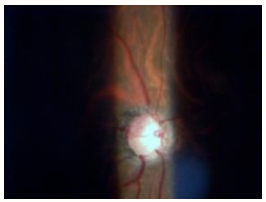


Appositional closure

PAS closure

↑ IOP (acute and/or chronic)

PACG



# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

## Disease - important health problem
## 重要健康问题

- 67 million primary glaucoma worldwide (50% PACG)

- PACG accounts for 25% of all glaucomatous optic neuropathy worldwide, and 50% of bilateral glaucoma blindness (optic nerve damage , corneal decompensation, cataract)
- PACG占全球所有的青光眼性视神经病变25％, 50％的双边青光眼失明（视神经损伤，白内障，角膜失代偿）

- Major form of glaucoma in Asia (prevalence: 2.90%)

# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

- Disease - important health
  - 重要健康问题

- Population-Based Survey in Tongliao, Inner Mongolia
- Subjects ≥ 40 yrs randomly selected from the population
- 5197 subjects examined
- Prevalence of PACG 1.42%

  – *Ophthalmology June 2011*

# Screening procedure
# 筛查程序

- Whom to screen?
  - Whole population?全民?
  - Age > 40?
  - Hypermetropia?
  - Positive family history?阳性家族史?
  - Opportunistic screening?

# Screening procedure
# 筛查程序

- What to screen?
  - Risk factors (危险因素)
    - Occludable angle (可闭塞的排水内角)- prerequisite (先决)for PACG
      - Angle status (排水内角状态)
      - AC depth (前房深度)
      - Axial length (眼轴长度)

# Screening procedure
# 筛查程序

Occludable angle (可闭塞的排水内角)

– Definition: $<180^0$ trabecular meshwork (小樑) visualized

– How to screen for occludable angle?

(如何筛查occludable角?)

# Sensitivity and Specificity
## 敏感性和明确性

- **Sensitivity** -ability to identify (识别能力) positive results (% of subjects correctly identified(正确识别) as having angle closure)
- **Specificity** –ability to identify negative results (% of open angle subjects correctly identified as not having angle closure
- 100% sensitivity = predict(预测)all people with occludable angle (-ve result means absence of occludable angle, low false -ve)
- 100% specificity = not predict anyone with open angle as occludable angle (+ve result means presence of occludable angle, low false +ve)

# Sensitivity and Specificity
## 敏感性和明确性

- High sensitivity- specificity low (even non-diseased subjects caught)
- True positive: Angle closure correctly diagnosed angle closure
- False positive: Open angle incorrectly identified as angle closure
- True negative: Open angle correctly identified as open angle
- False negative: Angle closure incorrectly identified as open angle

# Basic criteria for screening programme
# 筛查程序基本准则

- High sensitivity to ensure patients with occludable angles not missed
- High specificity to ensure that ophthalmic departments are not overwhelmed with unnecessary referrals of open angle patients (高特异性，以确保不与开角患者不必要的转介令眼科部门不堪重负)
- The British Diabetic Association proposed that any screening programme for diabetic retinopathy should have at least 80% sensitivity and specificity

# Screening for Angle Closure Glaucoma

## 筛查闭角型青光眼

Screening procedure – acceptable to public and health care professionals

筛查程序公众及医护人员可接受

- Goniscopy


Gold standard of angle examination and the appropriate test for diagnosing angle closure

标准的角度检查和相应的测试诊断闭角

# Screening for primary angle closure glaucoma
## 筛查闭角型青光眼

Gonioscopy

- Differentiate between (分辨) appositional and synechial closure

- Skill-dependent 技能的依赖
- Time-consuming 耗时
- ‘Invasive’
- Subjective主观

# Biometric measurements

Non-gonioscopic screening for occludable angle

**A shallow AC is strongly associated with angle closure**

一个浅的前房是与闭角紧密联系在一起的

**AC depth as an indicator for occludable angle**

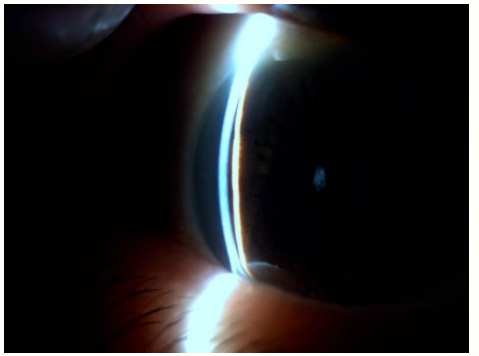
前房深度作為occludable angle的指标

# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

## Screening procedure – acceptable to public and health care professionals

## 筛查程序公众及医护人员可接受

- Non-gonioscopic methods for detection of occludable angle
  - Oblique flash light test
  - Van Herick's test utilizing the slit lamp -thickness of the cornea compared to depth of peripheral AC



- Low sensitivity: 45.5% and 61.9% - limited use as screening tests (作为筛选试验使用有限制) for occludable angles

»

*Aust N J Ophthalmol 1996 Aug*

# Non-gonioscopic method for detecting occludable angle

## AC Depth

- Optical pachymetry
- Accurate and reproducible 准确，重现性好

- Limitations (限制):
  - Bulky equipment and operator skill dependent 笨重的设备和操作人员的技能依赖
  - Not ideal for screening 不是理想的筛选
  - Sensitivity/specificity vary with different populations (85%/84% Mongolian, 75.6%/73.7% Singapore Chinese) 灵敏度/特异性随不同人群改变

- *Arch Ophthalmol Feb 2000*
- *Am J Ophthalmol May 2006*

# Non-gonioscopic method for detecting occludable angle

## Limbal Chamber Depth (LCD)

LCD measurement using van Herick test detects occludable angle better than ACD measurement in Singapore Chinese (sensitivity 83%, specificity 88.1%)

- LCD测量检测在新加坡的中国人occludable angle优于ACD的测量

»

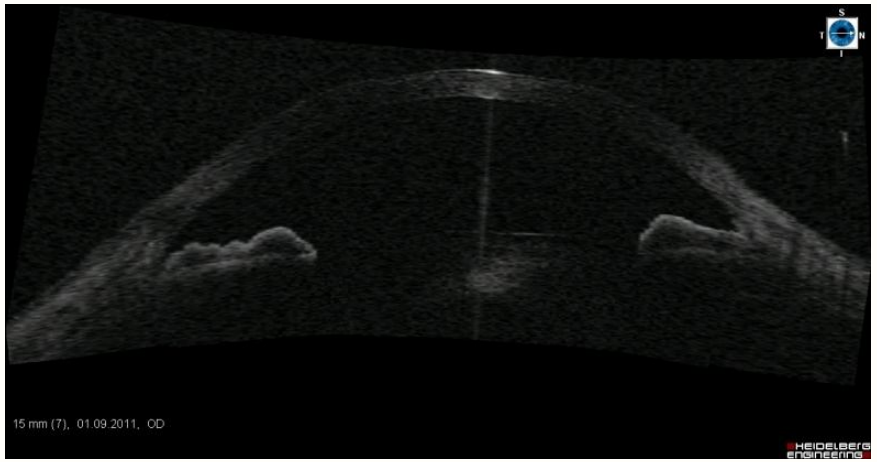
*Am J Ophthalmol May 2006*

# Biometric Measurements

| | Normal<br>Mean(SD) | Occludable angle<br>Mean(SD) |
|---|---|---|
| **Axial length (mm)** | 22.76 (0.78) | 22.07 (0.69) |
| **ACD (mm)** | 3.00 (0.30) | 2.53 (0.26) |
| **Lens thickness (mm)** | 4.31 (0.31) | 4.40 (0.53) |
| **Lens thickness/axial length ratio** | 0.192 (0.01) | 0.199 (0.02) |

# Screening method
# 筛查

- Imaging for biometric measurements

# Biometric measurements

- Handheld ultrasound biometer
- 3979 subjects

| | ACD (mm) | Axial length (mm) |
|---|---|---|
| Normal | 2.85 ± 0.39 | 22.62 ± 0.90 |
| Occludable angle | 2.55 ± 0.69 | 22.08 ± 0.83 |
| PACG | 2.48 ± 0.22 | 22.02 ± 0.59 |

*Optom Vis Sci Jan 2011*

# Biometric measurements

AS-OCT
1922 subjects

| | AC area | AC volume |
|---|---|---|
| Normal | 21.1mm$^2$ | 142.1mm$^3$ |
| Narrow angle | 15.6mm$^2$ | 97.6 mm$^3$ |

*Arch Ophthalmol May 2011*

# Screening methods using biometric measurements

- AS-OCT , SPAC, IOL master
- Limitations:
  - Low specificity (<77.7%)
  - Poor definition of scleral spur 巩膜突的定义差
  - Machine dependent 机依赖

# Screening methods using biometric measurements

- UBM measured anterior and posterior chamber
  - AAD- angle to angle distance
  - SSD-sulcus to sulcus distance
- Smaller in PAC than control
- Measurement independent to scleral spur (无需依靠巩膜突)

*J Med Assoc Thai May 2011*

# Screening methods using biometric measurements

- 461 subjects
- UBM measured angle-opening distance (AOD) at 500 µm from scleral spur , trabecular-iris angle (TIA), and trabecular-ciliary process distance (TCPD), iris thickness under light and dark conditions

- Good for detecting occludable angle

- Cut off values (切断値)
  - AOD500 0.17mm ⇒sensitivity 82% & specificity 96%
  - TIA 15.2 degrees ⇒ sensitivity 83% & specificity 93%

*Am J Ophthalmol Jun 2011*

# Screening methods using biometric measurements

- 30 eyes
- UBM measured ACD and lens thickness (LT) (晶體的厚度)

- IOL Master measured AL
- Relative lens position (RLP) = 10 × (ACD + 0.5 LT) /AL
- Decrease in RLP is predictive of appositional closure for narrow-angle eyes under dark conditions (黑暗条件下的RLP减少预测闭窄角眼appositional closure)

*Jap J Ophthalmol Apr 2011*

# Screening methods using biometric measurements

- 102 Chinese subjects
- AS OCT measurer lens vault (LV) (晶体拱顶)
- - perpendicular distance between anterior pole of lens and horizontal line joining the 2 scleral spurs
- A-scan biometry measured lens thickness (LT)
- LP (lens position) = ACD +1/2 LT
- RLP (relative LP) = LP/AL
- Thicker lenses and greater LV in narrow angle

» *Ophthalmology Mar 2011*

# Screening methods

- 996 Chinese subjects
- Adult height (成人高度)
- After controlling for age and gender, adult height was significantly related to anterior chamber depth but not significantly related to gonioscopic angle width
- 在控制为年龄和性别以后，成人高度显著与前房间深度有关，但不显著与gonioscopic角度宽度有关

– *Eye Sept 2009*

# Screening method for PACG
# 筛查闭角型青光眼

**More research is required to develop alternative screening tests (需要更多的研究开发替代的筛选试验):**

High sensitivity 高灵敏度

High specificity 高特异性

Reproducibility 重复性

Performance by paramedical staff 辅助人员可进行

Objective 客觀

Cost effective 成本效益

Non-invasive 非侵入性

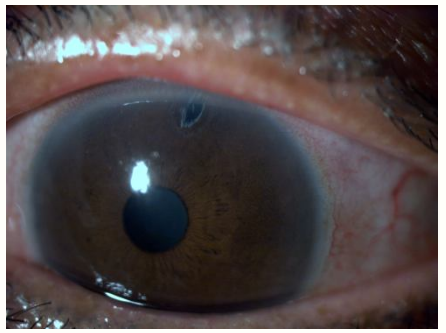
Simple and fast 简单而快速

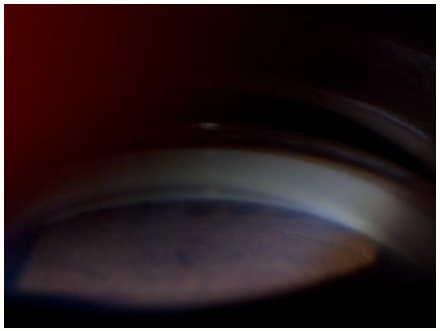
# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

**Treatment - safe, effective and universally agreed**

治疗安全有效及世界认同

- Laser PI
- ALPI
- Lens extraction





# Prophylactic treatment to prevent the development of PACG

- **Is the natural course of the disease adequately understood?** (对PACG自然过程认识足够吗?)

- Longitudinal studies: 20% occludable angle eyes progressed to PACG in 3-5 years (纵向研究：20％occludable角度眼睛在3-5年内发展到PACG)
- Not able to identify whom with occludable angle will progress to PACG (无法确定occludable角度为将进展到PACG)
  - By treating all people who have occludable angles with prophylactic LPI ⇒ will treat some people who will never develop PACG (对所有occludable角度的人都与预防性LPI⇒有些永远不会发展PACG的人亦要接收LPI)
  - *Am J Ophthalmol 1993*
  - *Acta Ophthalmol Scan 2003*

# Efficacy of prophylactic LPI

预防性治疗的成效

- **Is prophylactic LPI effective?** (预防性LPI成效?)

- Published evidence lacking to tell whether LPI is effective at preventing AAC, PAC, and PACG from developing in individuals with occludable angle
- 公布的证据缺乏判断LPI是否有效防止occludable angle发展成PACG
  Racial/ethnic variations in response to LPI
- 不同种族对LPI不同反应

– *Jiang Y Ophthalmic Epidemio 2010-results pending*

# Efficacy of prophylactic treatment
## 预防性治疗的功效

- LPI
  - Not always alleviate irido-trabecular apposition since mechanisms other than pupillary block may be present, such as plateau iris or phacomorphic angle closure
  - (并不能缓和全部angle closure因有non-pupillary block存在)
- ALPI- ?
- Lens extraction晶体摘除
  - Insufficient evidence for deciding which PACG patients should undergo lens extraction alone
- 证据不足以决定哪些PACG的患者应单独进行晶状体摘除

# Efficacy of prophylactic treatment
## 预防性治疗的成效

- 469 Caucasian phakic eyes with apposition or PAS angle closure
- LPI done
- Mean follow-up 8.5 ± 5.53 years
- 38.7% -increased IOP(眼壓上升)and 17.3% required medication(需降眼压药物)

*Can J Ophthalmol Jun 2011*

# Screening for primary angle closure in Mongolia

在蒙古的闭角型青光眼筛查

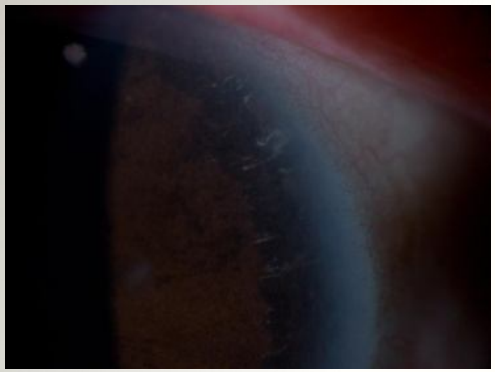
- **Randomized controlled trial to determine whether screening and prophylactic LPI will reduce the incidence of PACG in an East Asian population**
- 闭角型青光眼筛查和预防性**LPI**研究

- 4725 individuals aged ≥50 years recruited and randomized to LPI or no treatment (招募和随机LPI或不治疗)
- Unable to identify a reduction in the 6 year incidence of PACG after screening with ACD < 2.53 mm and prophylactic LPI of PAC
- (六年PACG发病率并设有因筛查和预防性LPI而减少)

- *B J Ophthalmol Mar 2003*
- *Br J Ophthalmol Nov 2010*

# Complications (并发症)of prophylactic treatment

- LPI – corneal, lens injury
- ALPI – long-term effects on angle?
- Lens extraction - risks of surgery, loss of accommodation



# Screening for Angle Closure Glaucoma
# 筛查闭角型青光眼

## Economic cost of early diagnosis and treatment
## 及早确诊和治疗经济成本

- Is the economic impact of a person‘s blindness from PACG balanced against the health costs incurred by screening and treatment?
- 及早确诊和治疗经济成本是否少于致盲后所需的社会照顾成本?

- A thorough cost effectiveness analysis is not available at present
- 目前没有一个全面的成本效益分析

# Cardinal Principles for Disease Screening (WHO)

## 世卫指引筛查疾病重要原则

1. Disease - important health problem with recognizable pre-symptomatic state (疾病 - 具有可识别的症状前的状态的重要健康问题)√
2. Screening procedure – acceptable to public and health care professionals (筛选程序 -被公众和医护人员接受)?
3. Treatment - safe, effective and universally agreed (治疗 - 安全，有效和普遍同意)?
4. Economic cost of early diagnosis and treatment – less than total health care expenditure for leaving the disease untreated (早期诊断和治疗的经济成本 少於病未处理的健康保健支出总额?

# Screening for PACG
# 筛查闭角型青光眼

- No universal agreed screening method (没有普遍同意的检查方法)
- Inability to identify eyes that actually develop PACG (无法确定实际开发PACG的眼睛)
  - Only 20% narrow angle eyes developed PAS/OHT in 3-5 years
- Doubtful effectiveness of prophylactic LPI in preventing PACG in eyes with occludable angle (预防性LPI的有效性成疑)
- Optimal screening test criteria are not yet known (优化筛选试验标准尚未清楚)
- *Am J Ophthalmol 1993 (115)*
- *Acta Ophthalmol Scan 2003 (81)*

# Screening for PACG
# 筛查闭角型青光眼

- More research is needed for the implementation of the best population-based screening program for PACG (最好的人口为基础的筛查方案的实施还需要更多的研究)
- The best evidence to date suggests:
  - Screening of high-risk subgroups may be more cost-effective than screening the entire population (筛查高风险的分组可能会高于整个人口筛选成本效益)
- Each society should determine its own criteria for the allocation of an affordable amount of resources for PACG screening
- 每个社会应确定分配的资源量能负担自己的标准为PACG筛查